DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
555 Winderley Pl., Ste. 200
Maitland, Fl 32751

VIA FEDERAL EXPRESS

WARNING LETTER
(CORRECTION)

FLA-00-14

December 15, 1999

Michael J. Murphy, Chief Operating Officer
International Sterilization Laboratory Corporation
217 Sampey Road
Groveland, Florida 34736

Dear Mr. Murphy:

We are writing to you because on October 20 through 25, 1999 FDA Investigator R. Kevin Vogel collected information that revealed serious regulatory problems involving your firm's contract sterilization of various medical devices.

Under the Federal Food, Drug, and Cosmetic Act (the Act), the products that your firm sterilizes are considered to be medical devices that are used to diagnose or treat medical conditions or to affect the structure or function of the body. The law requires that manufacturers conform to the Quality System (QS) regulations for medical devices, as specified in Title 21, Code of Federal Regulations (CFR), Part 820.

The inspection revealed that devices that you sterilize are adulterated within the meaning of section **501(h)** of the Act, in that the methods used in, or the facilities or controls used for the manufacture, packing, storage, or installation are not in conformance with the QS regulation. These violations include, but are not limited to the following:

QS Regulation/GMPs

1. Failure to conduct and/or document quality audits to assure that the quality system is in compliance with established requirements and is effective as required by 21 CFR 820.22. For example, there are no records documenting past quality audits having been conducted or that quality audits are conducted on a 6 month schedule as required by your firm's own written procedures. The quality audits also fail to include major production systems, i.e., calibration and maintenance of equipment (FDA 483, Item #6).

2. Failure to adequately validate sterilization chambers #s A & D as required by 21 CFR 820.75. For example, documentation for empty chamber studies is incomplete or missing. Temperature ranges are not adequate or were not set at appropriate set points during the validation process. Lack of documentation recording aeration room qualification and the number of thermocouples employed during qualification (FDA 483, Item #1A-E & #4).

3. Failure to establish and document all maintenance and calibration for each piece of processing or measuring equipment as required by 21 CFR 820.72. For example, there are no established procedures or records documenting procedures, schedules and action taken (FDA 483, Item #2).

4. Failure to investigate and document the cause of nonconformities related to quality systems including process and validation cycle deviations as required by 21 CFR 820.100(a)(2). For example, the investigation of BI positives found in two cycles was not documented and the effect of deviations was not determined. During a sterilization cycle the initial vacuum was out of specification, no record of the investigation was made. No documentation for 2 of 21 thermocouples that displayed readings outside of established specifications was made nor was there a determination of the effect on the adequacy of the cycle (FDA 483, Item #7).

5. Failure to establish and maintain written procedures for Corrective and Preventive Action (CAPA) [21 CFR 820.100], Change Control [21 CFR 820.100(a)(5)], and Management Review [21 CFR 820.20(c)] (FDA 483, Item #8).

6. Failure to establish and maintain procedures to ensure that all purchased or otherwise received product conforms to specified requirements as required by 21 CFR 820.50. For example, Certificates of Analysis received from suppliers of sterilization gases have not been verified and documented (FDA 483, Item #9).

7. Failure to establish and document production processes to ensure that device characteristics conform to specifications as required by 21 CFR 820.70(a). For example, transfer times from preconditioner to sterilizer are not defined and documented (FDA 483, Item #10).

The specific QS/GMP violations noted in this letter and in the List of Observations (FDA 483) issued to you at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

We are in possession of your response dated November 23, 1999 consisting of copies of records and logs documenting various tests and measurements conducted by your firm. Without the associated protocols, procedures and specifications these documents relate to, we cannot complete our review and determine their adequacy. The documents will be made part of the Florida District establishment file.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the awards of contracts. Additionally, no premarket submissions for devices to which QS regulation deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates for Products for Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of any steps you may have taken to correct the noted violations, including (1) the time frames within which the corrections will be completed if different from those annotated on the FDA 483, (2) any documentation indicating the corrections have been achieved, and (3) an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur.

Your response should be sent to Timothy J. Couzins, Compliance Officer, Food and Drug Administration, 555 Winderley Place, Suite 200, Maitland, Florida 32751, (407)475-4728.

Sincerely,

Douglas D. Tolen/ELH

Douglas D. Tolen
Director, Florida District